REMARKS

I. Introduction

By the present Amendment, claims 84 and 135-138 have been amended. Claims 1-73 and 96-127 have been cancelled. Accordingly, claims 76, 82-95, 131, 132, 134-138 remain pending in the application. Claims 135-138 are independent.

II. Office Action Summary

In the Office Action of October 31, 2005, claims 76, 82-95, 131, 132, and 134-138 were rejected under 35 U.S.C. §112, second paragraph. Claims 76, 82, 87-95, 131, 132, 134-135 were rejected under 35 U.S.C. §102(b) as being anticipated by Ostrem et al. ("Ostrem"). Claims 76, 82-95, 131, 132, and 134-138 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ostrem in view of U.S. Patent 6,240,374 to Cramer et al. ("Cramer"). These rejections are respectfully traversed.

III. Rejections Under 35 USC §112

Claims 76, 82-95, 131, 132, and 134-138 were rejected under 35 U.S.C. §112, second paragraph as being incomplete for omitting essential steps, resulting in a gap between the claimed steps. Regarding this rejection, the Office Action states that independent claims 135-138 each recite a step of constructing a first test peptide library comprising a plurality of first test peptides identified using the space-filling design. The Office Action indicates, however, that the claim recites a step of performing a space filling design of the parameterized peptides, and that such a step does not (explicitly) result in segregating predetermined peptides into "identified" or "not identified"

groupings. With respect to claim 84, the Office Action indicates that the limitation of a "sequence specific parameter" lacks proper antecedent basis. Regarding the remaining claims, it is presumed that they are likewise rejected for being dependent on a rejected base claim.

By the present amendment, Applicants have amended claims 84 and 135-138 to specifically address the issues raised in the Office Action under 35 U.S.C. §112, second paragraph. More particularly, claim 84 has been amended to properly reference a "second parameter" as recited in independent claim 135. Additionally, independent claims 135-138 have been amended to explicitly recited that the space-filling design results in identification of first test peptides.

Applicants therefore respectfully submit that, as amended, the presently pending claims satisfy the requirements of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of this rejection is respectfully requested.

IV. Rejections Under 35 USC §102

Claims 76, 82, 87-95, 131, 132, and 134-138 were rejected under 35 U.S.C. §102(b) as being anticipated by Ostrem. In regards to this rejection, the Office Action alleges that Ostrem discloses all of the steps recited in the claims. With respect to independent claim 135, the Office Action alleges, in particular, that Ostrem discloses the steps of deriving a quantitative relationship between the indicia of activity, the first parameter, and the second parameter; calculating an estimated indicia for each remaining peptide from the predetermined set of peptides using the quantitative relationship; setting a test requirement having a test indicia range; and selecting a

second test peptide library containing second test peptides ... wherein the second test peptides are not in the first test peptide library. Applicants respectfully disagree.

As to the requirements for supporting a rejection under 35 U.S.C. §102, Applicants first point out that the burden falls on the Examiner to establish a *prima facie* case of anticipation. See *In re Sun*, 31 USPQ2d 1451, 1453 (Fed. Cir. 1993). As emphasized by the court in *In re Warner*, "[t]he precise language of 35 U.S.C. 102 that "a person shall be entitled to a patent unless," concerning novelty and unobviousness, clearly places a burden of proof on the Patent Office which requires it to produce the factual basis for its rejection of an application under sections 102 and 103. . . ." (Emphasis added) 154 USPQ 173, 177 (C.C.P.A. 1967), *cert. denied*, 389 U.S. 1057 (1968).

In order to qualify as an anticipatory reference, a prior art reference must necessarily disclose each and every element recited in the claimed invention. This disclosure must also be made with a sufficient level of clarity. See *Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 43 USPQ2d 1481, 1490 (Fed. Cir. 1997). See also *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("[T]he [prior art] reference must describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it." (citations omitted)). As further stated by the Federal Circuit, "Although this disclosure requirement presupposes the knowledge of one skilled in the art of the claimed invention, that presumed knowledge does not grant a license to read into the prior art reference teachings that are not there." (Emphasis added) *Id.*

Reference is further made to the decision of *In re Robertson*, 49 USPQ 2d 1949 (Fed. Cir. 1999), wherein the court pointed out that anticipation under 35 U.S.C. §102 requires that each and every element as set forth in the claim be found, either expressly or inherently described in a single prior art reference. As noted by that court, if the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if the element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." (Emphasis added). Moreover, the court pointed out that inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. See also *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (C.C.P.A. 1981) ("Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.")

Finally, the alleged anticipatory reference must be enabling. In particular, it is the claimed invention that must be enabled within the reference and not any other teachings disclosed by the reference. See *Elan Pharms. Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 68 USPQ2d 1373, 1375-76 (Fed. Cir. 2003) ("To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate."); and *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003) ("A claimed invention cannot be anticipated by a

prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.").

Turning now to the instant invention, independent claim 135 defines a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The method comprises, in part, the steps of:

...

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;

calculating an estimated indicia for each remaining peptide from said predetermined set of peptides using said quantitative relationship;

setting a test requirement, based on a desired activity, having a test indicia range;

selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

measuring the indicia of each second test peptide; and

identifying at least one second test peptide having a measured indicia that satisfies said test requirement.

According to independent claim 135, a predetermined set of peptides is identified and parameterized. A space-filling design is then performed for the parameterized peptides that will be used in constructing a first test peptide library. Next, each first test peptide is tested so that an indicia can be measured for a desired activity.

According to at least one feature of independent claim 135, a quantitative relationship is derived based on three specific properties: the measured indicia, the first parameter, and the second parameter. Once the quantitative relationship is

determined, it is applied to calculate (i.e., compute) an estimated indicia for each remaining peptide from the predetermined set of peptides. It is noted that these peptides were not part of the first test peptide library. A test requirement is subsequently set based on the desired activity level. The test requirement is in the form of a range of test indicia values. These values can correspond to a desired range that satisfies a criteria considered to be important. Next, a second test peptide library containing at least one second test peptide is selected. Only second test peptides having an estimated indicia that has been calculated to satisfy the test requirement are selected to be in the second test peptide library. Since the estimated indicia are calculated only for the remaining peptides, none of the second test peptides are present in the first test peptide library. Furthermore, none of the second test peptides have been tested (e.g., screened or assayed) as this time. At this point the second test peptides are tested in order to actually measure the indicia. Finally, at least one second test peptide having a measured indicia that satisfies the test requirement is identified.

The method defined by claim 135 advantageously reduces the amount of experimentation required to identify peptides having a desired indicia as discussed in the "Background" section of the application. This reduction can directly translate to a reduction in time and costs associated with identifying such peptides. Additionally, it is possible to generate a substantially large group of candidate peptides that could potentially have an indicia which satisfies the test requirement. As can be appreciated, it is not cost effective, efficient, or convenient to test a large number (e.g., over one million) peptides. The candidate peptides can then be filtered to a smaller number of second test peptides that will actually be tested by properly setting the test requirement.

Consequently, the number of actual experiments conducted can be significantly reduced.

Ostrem fails to disclose or suggest each and every step for a method of identifying peptides with a desired activity, as set forth in independent claim 135. In fact, Ostrem fails to provide a disclosure sufficient for enabling one skilled in the art to identify peptides having a desired activity by performing all the steps recited in independent claim 135. Ostrem discloses a library for screening of biotinylated factor Xa-SAP mixture added to library beads. Beads that showed a blue color were destained, stripped, and further screened with the factor Xa-SAP-inhibitor mixture. At best, Ostrem identifies certain factor Xa inhibitors from an initial combinatorial library based on results obtained by assaying the beads.

In contrast to the claimed invention, Ostrem does not perform essential steps such as performing a space-filling design and constructing a first test peptide library. Applicants' review of Ostrem has failed to identify any evidence that Ostrem was actually attempting to construct a first test peptide library designed to provide any organized representation of, for example, the total octamer space. Ostrem does not even appear to mention of a space-filling design or provide some suggestion for a design that selects representatives from a plurality of compound isomers. The most comprehensive listing of peptides in Ostrem appears to be presented in Table 1, which does not include any peptide isomers (comprised of the same amino acids but varying in sequence). Ostrem itself discloses that a complete representation of peptides in the library was not known, as only a select few peptides were confirmed as being available after activity assays were completed. ("Beads picked from the library which showed no

staining when incubated with active-site inhibited factor Xa under these conditions were briefly stripped and destained, then incubated with uninhibited factor Xa and SAP. Beads which restained were submitted for sequencing by Edman degradation. Peptides were resynthesized based on sequences obtained from individual beads." Page 1054, col.1, lines 45-51).

Another indication that the complete set of peptides in Ostrem's library screening procedure was not known is the "split-synthesis methodology" used to generate the peptides. As is known, such methods are often used when the intent is to screen first and confirm the presence of peptides later. Typically, split synthesis methods are used when the goal is to synthesize and assay large libraries of peptides in a batch format. Such an approach does not attempt to take advantage of group isomers and does not attempt to account for any specific peptide(s) before assaying. Indeed the cost and time associated with confirming each peptide in the test library is prohibitive. Ostrem's selection of the split-synthesis method clearly shows that a space-filling design was not applied.

Ostrem also fails to disclose the claimed feature of parameterizing the predetermined peptides through determination of first and second parameters. Determining a peptide length of 8 amino acids simply cannot be interpreted as reading on the claimed the step of determining a second parameter which depends on the specific order of constitutive subunits within each desired peptide. The only measurements taken by Ostrem appear to relate to the potency of the peptides. This value, however, is different from the first and second parameters measured in the

claimed invention, and in fact appears to be more consistent with measurement of an activity level.

Similarly, Ostrem provides no disclosure or suggestion for deriving a quantitative relationship between the measured indicia, the first parameter, and the second parameter. Finally, Ostrem clearly fails to even remotely suggest application of any derived quantitative relationship to calculate an estimated indicia for peptides remaining in the predetermined set of peptides. In fact, Ostrem appears to be completely silent on when, or how, this specific step is performed, particularly in view of the fact that no quantitative relationship is ever derived. Rather, Ostrem measures the increased potency range of the initial leads identified in the combinatorial library. They are not calculated from a derived relationship as set forth in the claims.

The Office Action alleges that Ostrem describes procedures for testing a family of combinatorial peptides of eight amino acids in length to bind factor Xa and the level of the potency. The Office Action concludes that this description reads on the claimed step of determining a relationship between an indicia of activity, a first parameter, and a second parameter. The Office Action boldly makes this allegation without providing any support or explicit reference to where, in Ostrem, it is stated or even hinted that a quantitative relationship is ever derived. Review of Ostrem reveals only one thing. Various amino acids on peptide bound beads are assayed in order to measure inhibition of factor Xa activity.

Ostrem appears to have assayed peptides attached to the same beads used in synthesis. In contrast, all of the screening applicable to the claimed invention uses peptides cleaved from the solid support. Peptides in their free form can be assayed for

performance "in solution" and "immobilized to standard tissue culture surfaces. It is difficult to see how Ostrem could have used peptides attached to a synthesis resin in a screen for compounds intended to enhance culture media. It is even more difficult to see how one skilled in the art could have applied the methods of Ostrem to the development of a process for enhancing culture media. In many cases peptides in a cell culture environment must cross the cell outer membrane before having an impact. The contribution from a peptide immobilized to a synthesis bead would certainly be biased.

Applicants further submit that testing of peptides attached to the same beads is a far cry from derivation of an actual quantitative formula that can be used to model the relationship between the indicia, first parameter, and second parameter, as set forth in the claimed invention. Ostrem does not provide any indication of how the inhibition of factor Xa activity relates to the first parameter or the second parameter. Furthermore, Ostrem never discusses a single formula that has been derived or any values that are calculated (not measured through assays) using this formula.

The Office Action also appears to be completely silent on identifying where Ostrem actually discloses the step of calculating an estimated indicia using the derived relationship. Again, Ostrem merely measures quantities such as the inhibition of Xa activity. These measurements are subsequently plotted in various graphs. Ostrem does not contain a single quantitative formula that is representative of these graphs. Furthermore, Ostrem appears to be completely silent on applying a quantitative formula to predict the potency of untested peptides.

The Office Action alleges that Ostrem discloses the step of setting a test requirement based on a desired activity. In support of this rejection, the Office Action indicates that Ostrem provides four separate assays that are performed on peptides identified from an initial set. The selection of these peptides allegedly reads on the step of setting a test requirement.

This particular analogy appears contrary to the claimed steps, and actually teaches away from the present invention. As set forth in the disclosure, once a quantitative relationship has been derived, an estimated indicia is calculated (using the derived relationship) for peptides that have not been previously screened. Calculation of the estimated indicia is intended to reduce the number of test/assays performed. This allows consideration of an extremely high number of peptides in determining those which may have the desired level of activity.

By the Office Action's own admission, Ostrem does exactly the opposite. Specifically, as indicated in the Office Action, Ostrem performs four separate assays of peptides identified from the initial set. It is unclear of how performing assays of peptides could possible read on, or even remotely suggest, calculating an estimated indicia using a derived quantitative relationship. Furthermore, the estimated indicia is calculated for peptides that remain from the predetermined set of peptides, i.e., peptides which are not included from the first test peptide library and have not yet been tested. In contrast, Ostrem never goes outside the original combinatorial library to identify peptides that have not been assayed and calculate an estimated value for the inhibition factor of Xa activity prior to performing an assay. In fact, Ostrem is completely silent about

calculating and/or estimating any values. Applicants note that silence cannot be construed by the Office Action as actually disclosing a claimed step.

Additionally, the step of setting a test requirement is intended to identify candidates that have an estimated indicia which satisfies a desired level of activity. Accordingly, the test requirement must necessarily be set prior to testing the peptides. As indicated in the Office Action, the peptides in Ostrem are selected as a result of the assay.

There simply is no disclosure, or even suggestion, in Ostrem to indicate that a quantitative relationship is ever derived and subsequently applied to estimate parameters such as the inhibition of factor Xa activity prior to performing an assay of the peptide bound beads. Thus, there can be no realistic analogy to the claimed invention. Further, there are not citations to the exact location where Ostrem allegedly discloses the steps recited in the claimed invention. As previously indicated, an anticipatory reference must be enabling and must disclose all the claimed steps. The entire anticipation analysis presented in the Office Action appears tantamount to an application of the claims themselves as a blueprint to sustain and justify the rejection.

In response to Applicants previous arguments, the Office Action indicates that tables 1 and 2, and Figures 1 and 2 of Ostrem clearly demonstrate the estimation of curves for peptides exhibiting inhibition of factor Xa activity among tested peptide sequences identified as binding factor Xa and increased potency. This is clearly not the case, as the "demonstration" itself appears to be somewhat perplexing.

At the outset, Applicants note that the claimed invention is not directed to the estimation of curves. This fact is clearly established in the preamble and recited steps

of the claims. Ostrem plots test results on a graph and draws a curve between adjacent points. Such techniques are taught in elementary/high school classes using drawing devices such as, for example, French curves. This is entirely different from actually deriving a relationship that can be applied to compute and estimate values for untested peptides. The Office Action attempts to trivialize the complexities associated with quantitative modeling of data and systems. There are entire fields of study devoted to such endeavors.

Further, the claimed invention specifically recites that the relationship is derived with respect to three specific properties: the indicia of the activity, the first parameter, and the second parameter. While Ostrem appears to plot the results of various tests on peptides that inhibit factor Xa activity, there does not appear to be any suggestion to relate the inhibition of factor Xa activity to either a first or second parameter. Ostrem simply fails to provide any disclosure or suggestion for a quantitative relationship that is in a form capable of being subsequently applied to estimate, for example, a value representative of the inhibition of factor Xa in untested peptides.

The Office Action goes onto to indicate that Ostrem demonstrates estimation curves for peptides exhibiting inhibition of factor Xa activity among tested peptides sequences. First, Ostrem does not demonstrate estimation of any sort. Second, there is no realistic purpose for estimating a value for the level of inhibition of factor Xa activity for peptides that have already been screened to measure an actual value for the level of inhibition of factor Xa activity.

Additionally, the Office Action indicates that the curves are estimated for discrete measurement which were then further extrapolated. It is unclear how Ostrem derives a

quantitative relationship or performs any sort of extrapolation that could possibly be construed as an estimation of untested peptide activity.

Ostrem, in fact, does not perform any extrapolation and never discusses, or even mentions, extrapolation of any type within his teachings. Figures 1-5 illustrate measurements that are plotted. A "best fit" curve, or line, appears to be drawn between the points that have been plotted on the graph. It is unclear how this disclosure can realistically be interpreted as an estimation of the activity of untested peptides using a derived relationship. The curve plotted between measurements is not even related to untested peptides. In fact, Ostrem provides no mention of the location where untested peptides would fall within any of the graphs. At best, extensive experimentation would be necessary to derive such a relationship.

This interpretation of Ostrem appears to be further evidence of the Office Action's failure to make a *prima facie* case of anticipation. More particularly, the Office Action has failed to identify any specific passages in Ostrem which state, or even remotely suggest, that a quantitative formula has been applied to estimate the inhibition of factor Xa by untested peptides. Rather, the Office Action generally refers to passages which describe the experimental procedure and broadly discuss the test results. Since Ostrem "clearly discloses" derivation and application of a quantitative relationship, it is unclear why the Office Action is unable to cite a single formula and discussion of its application to estimate the potency of untested peptides. Such information should be easily identifiable within the reference. Ostrem does not even discuss untested peptides. Ostrem appears to be only concerned with peptides that have been tested.

Applicants further note that while the initial peptides selected by Ostrem showed measurable performance characteristics when assayed in vitro, these same peptides failed to perform in their intended in vivo application and the core motif required further modification to yield a functional peptide. As stated by Ostrem, "[A]lthough potent in chromogenic activity assays and *in vitro* coagulations assays, initial experimental work looking at half-life in rats following *i.v.* bolus injections showed that *N*-acyl, *N*-akyl peptides were inactivated or cleared from plasma within1-2 minutes." See page 1057, column 1, lines 5-9. In contrast peptides derived from the claimed process are capable of performing in their intended application without further modification.

Ostrem simply fails to either disclose or suggest features that are explicitly recited in the claimed invention, such as:

> deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;
>
> calculating an estimated indicia for each remaining peptide from said predetermined set of peptides using said quantitative relationship;
>
> setting a test requirement, based on a desired activity, having a test indicia range;
>
> selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

It is therefore respectfully submitted that independent claim 135 is allowable over the art of record.

Claims 76 and 82-95 depend, either directly or indirectly, from independent claim 135, and are therefore believed allowable for at least the reasons as set forth above

with respect to independent claim 135. In addition, these claims each introduce novel elements that independent render them patentable over the art of record.

Independent claims 136-138 each recite steps that are somewhat similar to those recited in independent claim 135. These steps are also not shown or suggested by Ostrem. Specifically, each of these claims recites a step of deriving a quantitative relationship between the indicia of activity, a first parameter, and a second parameter. Additionally, these claims each recite a step that utilizes this derived quantitative relationship to calculate an estimated indicia for peptides that have not been tested. These claims also utilize the estimated indicia in setting a test requirement to identify peptides that will actually be tested. As previously discussed with respect to independent claim 135, Ostrem simply does not provide any disclosure or suggestion for these features.

It is therefore respectfully submitted that independent claims 136-138 are allowable over the art of record.

Claims 131, 132, and 134 depend from independent claim 137 and are also believed allowable for at least the reasons set forth above with respect to independent claims 135 and 137. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

V. Rejections Under 35 USC §103

Claims 76, 82-95, 131, 132, and 134-138 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ostrem in view of Cramer. Regarding this rejection, the Office Action contends that Ostrem discloses most of the features of the claimed

invention. Cramer is relied upon for disclosing various features not disclosed by Ostrem. Regarding claims 83-86, the Office Action indicates that Cramer sets forth a method of validating molecular structure descriptors that may be used to select optimally diverse subsets of molecules with a desired set of characteristics. The Office Action further indicates that Cramer discloses a library database of compounds that can be selected on the basis of molecular weight and hydrophobicity.

Applicants would like to point out that a *prima facie* case of obviousness must be made in order to support a rejection under 35 U.S.C. §103. According to the Federal Circuit and the M.P.E.P., a *prima facie* case of obviousness requires that three basic criteria be met. First, there must be some suggestion or motivation in the primary reference to modify, combine, or seek out the teachings of a secondary reference. Second, there must be a realistic expectation of success from combining the two references. Finally, the prior art references must clearly teach or suggest all the claim limitations. See M.P.E.P. §706.02(j). The Federal Circuit has consistently supported the requirements of the M.P.E.P. in stating, for example, that "[i]n proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992).

In the decision of *In re Fine*, 5 USPQ 2d 1596 (Fed. Cir. 1988), the court pointed out that the PTO has the burden under '103 to establish a *prima facie* case of obviousness and can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. As noted by

the court, whether a particular combination might be "obvious to try" is not a legitimate test of patentability and obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. The teachings of the prior art must be examined objectively, and not in view of the claimed invention. As further noted by the court, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

Furthermore, such requirements have been clarified in the decision of *In re Lee*, 61 USPQ 2d 1430 (Fed. Cir. 2002) wherein the court in reversing an obviousness rejection indicated that deficiencies of the cited references cannot be remedied with conclusions about what is "basic knowledge" or "common knowledge". The court pointed out:

> The Examiner's conclusory statements that "the demonstration mode is just a programmable feature which can be used in many different device[s] for providing automatic introduction by adding the proper programming software" and that "another motivation would be that the automatic demonstration mode is user friendly and it functions as a tutorial" do not adequately address the issue of motivation to combine. This factual question of motivation is immaterial to patentability, and could not be resolved on subjected belief and unknown authority. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher."... Thus, the Board must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency's conclusion. (emphasis added)

As previously discussed, Ostrem clearly fails to disclose numerous features recited in independent claims 135-138. The inclusion of Cramer as a secondary reference does nothing to remedy this shortcoming. In addition, Cramer does not appear to even disclose the features recited in claims 83-86, as alleged by the Office Action. Cramer discloses a method of creating and searching a library (i.e., database) of potential molecules using validated molecular structural descriptors. Cramer appears to be concerned only with the database and data structure used to store the records pertaining to the molecules. For example, Cramer illustrates a table which stores a set of properties in an encoded form representative of a shape descriptor. At least one of these properties is indicated as being the hydrophobicity of the molecule. However, Cramer is not concerned with the screening of peptides and/or determination of desired activities. Merely storing the value of this property as a parameter of a data structure cannot be construed as disclosing, or suggesting, any of the claimed features. In fact, Ostrem and Cramer do not even appear to be properly combinable for arriving at the claimed invention, because neither reference provides any motivation to seek out the teachings of the other with a realistic expectation of arriving at the claimed invention.

Even if Ostrem and Cramer were properly combinable, the combined teachings would be insufficient to render the claimed invention obvious. Cramer provides an overview of the use of compound libraries, while Ostrem provides a description for finding other low molecular weight peptide inhibitors of factor Xa. Neither the combination nor individual references teaches a method for finding compounds capable of enhancing cell culture media. As a specific example, neither Ostrem nor Cramer provides details as to the percentage of undefined hydrolysate that can be present in

media screening nor advantage gained with an adaptation culture. In both cases, support exists within the present specification

Consequently, there is absolutely no motivation for a skilled artisan reading the teachings of Ostrem to further seek out the teachings of Cramer with a realistic expectation of arriving at the claimed invention. Even is these two references where combinable, one would still fail to arrive at the claimed invention because Ostrem fails to disclose various steps recited in the independent claims, and Cramer fails to disclose various steps further recited in the dependent claims.

Accordingly, the presently pending claims are believed to be allowable over the art of record.

VI. Conclusion

For the reasons stated above, it is respectfully submitted that all of the pending claims are now in condition for allowance. Therefore, a Notice of Allowance is believed in order, and courteously solicited.

If the Examiner believes that there are any matters which can be resolved by way of either a personal or telephone interview, the Examiner is invited to contact Applicants' undersigned attorney at the number indicated below.

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AUTHORIZATION

Applicants request any shortage or excess in fees in connection with the filing of this paper, including extension of time fees, and for which no other form of payment is offered, be charged or credited to Deposit Account No. 01-2135 (Case: 1385.45510X00).

Respectfully submitted,
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